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=> s (solute (w) stress) and expression

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1 FILE LIFESCI  
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2 FILE WPINDEX  
1 FILE COMPENDEX  
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L1 QUE (SOLUTE (W) STRESS) AND EXPRESSION

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=> s l1

L2	6 FILE USPATFULL
L3	4 FILE INPADOC
L4	2 FILE BIOSIS
L5	2 FILE IFIPAT
L6	2 FILE WPIDS
L7	1 FILE BIOTECHDS
L8	1 FILE CAPLUS
L9	1 FILE FEDRIP
L10	1 FILE LIFESCI
L11	1 FILE COMPENDEX
L12	1 FILE INSPEC
L13	1 FILE EUROPATFULL
L14	1 FILE PATOSWO

TOTAL FOR ALL FILES

L15 24 L1

=> d l15 1-24 ibib abs

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L15 ANSWER 1 OF 24 USPATFULL

IN Maiorella, Brian, Oakland, CA, UNITED STATES  
Inlow, Duane, Oakland, CA, UNITED STATES  
Howarth, William, Richmond, CA, UNITED STATES

AB A method of determining the optimal level of product **expression**  
and cell growth of animal cell culture is described. The method

generally comprises culturing cells under conditions of **solute stress**, that is, under conditions whereby optimal cell growth or growth rate is decreased yet levels of product **expression** are increased. In a preferred embodiment of the invention is described a method of increasing the yield of monoclonal antibodies comprising culturing hybridoma cells in an environment of **solute stress**. One approach to the creation of such an environment is the addition of inorganic salts, organic polyols, or metabolic products to the culture medium. One- to three-fold increases in antibody yield have been obtained by these methods.

TI Method of increasing product **expression** through **solute stress**

L15 ANSWER 2 OF 24 USPATFULL

IN Maiorella, Brian, Oakland, CA, United States  
Inlow, Duane, Oakland, CA, United States  
Howarth, William, Richmond, CA, United States

AB A method of determining the optimal level of product **expression** and cell growth of animal cell culture is described. The method generally comprises culturing cells under conditions of **solute stress**, that is, under conditions whereby optimal cell growth or growth rate is decreased yet levels of product **expression** are increased. In a preferred embodiment of the invention is described a method of increasing the yield of monoclonal antibodies comprising culturing hybridoma cells in an environment of **solute stress**. One approach to the creation of such an environment is the addition of inorganic salts, organic polyols, or metabolic products to the culture medium. One- to three-fold increases in antibody yield have been obtained by these methods.

TI Method of increasing product **expression** through **solute stress**

L15 ANSWER 3 OF 24 USPATFULL

IN Inlow, Duane, Oakland, CA, United States  
Maiorella, Brian, Oakland, CA, United States  
Howarth, William, Castro Valley, CA, United States

AB Protein-free cell culture media supplements are described consisting of synergistic combinations of medium components, which when added to cell culture media, either serum supplemented or serum-free, enhance cell growth, culture longevity and product **expression**.

TI Cell culture medium for enhanced cell growth, culture longevity, and product **expression**

L15 ANSWER 4 OF 24 USPATFULL

IN Etcheverry, Tina, Berkeley, CA, United States  
Ryll, Thomas, San Mateo, CA, United States

AB The present invention relates to novel process for the preparation of glycoproteins by mammalian cell culture wherein the sialic acid content of the glycoprotein produced is controlled over a broad range of values by manipulating the cell culture environment. The invention provides for processes in which the sialic acid content of the glycoprotein is modified by changes in cell culture parameters which affect cell specific productivity. Preferred embodiments of the invention include cell culture processes in the osmolality of the cell culture is controlled as well as the concentration of a transcription enhancer during the production phase of the cell culture. The invention further provides for novel preparations of soluble type 1 tumor necrosis factor immunoglobulin G1 and their uses in the treatment of inflammatory or immune related disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Mammalian cell culture process for producing a tumor necrosis factor

receptor immunoglobulin chimeric protein

L15 ANSWER 5 OF 24 USPATFULL

IN Etcheverry, Tina, Berkeley, CA, United States  
Ryll, Thomas, San Mateo, CA, United States

AB The present invention relates to novel process for the preparation of glycoproteins by mammalian cell culture wherein the sialic acid content of the glycoprotein produced is controlled over a broad range of values by manipulating the cell culture environment. The invention provides for processes in which the sialic acid content of the glycoprotein is modified by changes in cell culture parameters which affect cell specific productivity. Preferred embodiments of the invention include cell culture processes in the osmolality of the cell culture is controlled as well as the concentration of a transcription enhancer during the production phase of the cell culture. The invention further provides for novel preparations of soluble type 1 tumor necrosis factor immunoglobulin G1 and their uses in the treatment of inflammatory or immune related disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Mammalian cell culture process

L15 ANSWER 6 OF 24 USPATFULL

IN Inlow, Duane, Oakland, CA, United States  
Maiorella, Brian, Oakland, CA, United States  
Shauger, Andrea E., Albany, CA, United States

AB This invention is in the field of cell and/or tissue culture. In particular, this invention relates to methods which adapt cells to a desired phenotype by exposing the cells to high levels of ammonia in culture, and subsequently transferring the adapted cells to a new culture medium in which there is no initial level of ammonia or the initial level of ammonia is below the level to which cells have been exposed to during the adaptation process. In this new culture medium, the adapted cells express the desired phenotype of growing to a higher viable cell density, and/or remaining viable for a longer period of time, and/or producing more of a desired cell product than their non-adapted counterparts grown in the same medium. This invention includes the adapted cells produced thereby and their cell products.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Methods for adapting cells for increased product production through exposure to ammonia

L15 ANSWER 7 OF 24 INPADOC COPYRIGHT 2002 EPO

INS MAIORELLA BRIAN; INLOW DUANE; HOWARTH WILLIAM

TI METHOD OF INCREASING PRODUCT **EXPRESSION** THROUGH **SOLUTE STRESS**

L15 ANSWER 8 OF 24 INPADOC COPYRIGHT 2002 EPO

INS MAIORELLA BRIAN; INLOW DUANE; HOWARTH WILLIAM

TI METHOD OF INCREASING PRODUCT **EXPRESSION** THROUGH **SOLUTE STRESS**

L15 ANSWER 9 OF 24 INPADOC COPYRIGHT 2002 EPO

INS MAIORELLA BRIAN; INLOW DUANE; HOWARTH WILLIAM

TI METHOD OF INCREASING PRODUCT **EXPRESSION** THROUGH **SOLUTE STRESS**

L15 ANSWER 10 OF 24 INPADOC COPYRIGHT 2002 EPO

INS MAIORELLA BRIAN; INLOW DUANE; HOWARTH WILLIAM

TI METHOD OF INCREASING PRODUCT **EXPRESSION** THROUGH **SOLUTE STRESS**

L15 ANSWER 11 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

SO Phytopathology, (June, 2002) Vol. 92, No. 6 Supplement, pp. S97-S98.

print.

Meeting Info.: 2002 Annual Meeting of the American Phytopathological Society Milwaukee, WI, USA July 27-31, 2002  
ISSN: 0031-949X.

AU Halverson, L. J. (1)

AB We have evaluated the ultrastructural properties of *Pseudomonas putida* biofilms and the transcriptional regulation of genes that are expressed during biofilm development under conditions of matric stress (low water content), **solute stress**, and when water is not limiting. Biofilms that formed under a matric stress produce significantly more exopolysaccharides and confocal scanning laser microscopy (CSLM) of gfp-tagged cells with the extracellular polysaccharide (EPS) stained with calcofluor revealed that most of the EPS was localized at the air-biofilm interface rather than distributed uniformly through the biofilm. CSLM also revealed that biofilms that develop under matric stress growth conditions are taller and more compact than those that form under **solute stress** conditions or when water is not limiting. Furthermore, we have identified numerous transcriptionally regulated genes whose **expression** is increased or decreased under matric stress conditions. These results suggest that a unique suite of adaptive traits are required for biofilm growth under low water content conditions and that they differ from those required for biofilm growth under **solute stress** conditions or when water is not limiting.

TI Biofilm development on surfaces in terrestrial habitats.

L15 ANSWER 12 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

SO Official Gazette of the United States Patent and Trademark Office Patents, (May 29, 2001) Vol. 1246, No. 5, pp. No Pagination. e-file.  
ISSN: 0098-1133.

AU Maiorella, Brian; Inlow, Duane; Howarth, William (1)

AB A method of determining the optimal level of product **expression** and cell growth of animal cell culture is described. The method generally comprises culturing cells under conditions of **solute stress**, that is, under conditions whereby optimal cell growth or growth rate is decreased yet levels of product **expression** are increased. In a preferred embodiment of the invention is described a method of increasing the yield of monoclonal antibodies comprising culturing hybridoma cells in an environment of **solute stress**. One approach to the creation of such an environment is the addition of inorganic salts, organic polyols, or metabolic products to the culture medium. One- to three-fold increases in antibody yield have been obtained by these methods.

TI Method of increasing product **expression** through **solute stress**.

L15 ANSWER 13 OF 24 IFIPAT COPYRIGHT 2002 IFI

INF Howarth; William, Richmond, CA, US

Inlow; Duane, Oakland, CA, US

Maiorella; Brian, Oakland, CA, US

IN Howarth William; Inlow Duane; Maiorella Brian

AB A method of determining the optimal level of product **expression** and cell growth of animal cell culture is described. The method generally comprises culturing cells under conditions of **solute stress**, that is, under conditions whereby optimal cell growth or growth rate is decreased yet levels of product **expression** are increased. In a preferred embodiment of the invention is described a method of increasing the yield of monoclonal antibodies comprising culturing hybridoma cells in an environment of **solute stress**. One approach to the creation of such an environment is the addition of inorganic salts, organic polyols, or metabolic products to the culture medium. One- to three-fold increases in antibody yield have been obtained by these methods.

CLMN 38 3 Figure(s).

FIG. 1 shows the effect of 400 mOsmol/kg media on antibody yields of human/human/murine trioma D-234 cells in serum-free HL-1 media. The

closed circles represent cell growth in 300 mOsmol/kg media and the open circles represent the resulting IgM antibody yield. The closed squares represent cell growth in 400 mOsmol/kg media and the open squares represent resulting IgM antibody yield.

FIG. 2 shows the effect of ammonium chloride on production of antibodies of D-234 cells. The closed circles represent cell growth in the absence of ammonium chloride and the open circles represent the resulting IgM antibody yield. The open triangles represent cell growth in the presence of 10 mM ammonium chloride and the closed triangles represent resulting antibody yield.

FIG. 3 shows the effect of sodium chloride on specific production rate of IgG antibody by hybridoma 454A12.

TI METHOD OF INCREASING PRODUCT **EXPRESSION** THROUGH **SOLUTE STRESS**

L15 ANSWER 14 OF 24 IFIPAT COPYRIGHT 2002 IFI

INF Howarth; William, Richmond, CA

Inlow; Duane, Oakland, CA

Maiorella; Brian, Oakland, CA

IN Howarth William; Inlow Duane; Maiorella Brian

AB A method of determining the optimal level of product **expression** and cell growth of animal cell culture is described. The method generally comprises culturing cells under conditions of **solute stress**, that is, under conditions whereby optimal cell growth or growth rate is decreased yet levels of product **expression** are increased. In a preferred embodiment of the invention is described a method of increasing the yield of monoclonal antibodies comprising culturing hybridoma cells in an environment of **solute stress**. One approach to the creation of such an environment is the addition of inorganic salts, organic polyols, or metabolic products to the culture medium. One- to three-fold increases in antibody yield have been obtained by these methods.

CLMN 21

GI 3 Drawing Sheet(s), 4 Figure(s).

TI METHOD OF INCREASING PRODUCT **EXPRESSION** THROUGH **SOLUTE STRESS**; AMPLIFICATION OF TRANSCRIPTION AND RECOVERY OF CONSEQUENT PROTEIN IN MAMMALIAN CELLS; MIX SUPPRESSOR SOLUTE AND PROPAGATING CELLS IN SOLUTION, RECOVER AND PURIFY PROTEIN FROM CELL CULTURE

L15 ANSWER 15 OF 24 WPIDS (C) 2002 THOMSON DERWENT

IN HOWARTH, W; INLOW, D; MAIORELLA, B

AN 2001-366475 [38] WPIDS

CR 1989-178386 [24]

AB US 6238891 B UPAB: 20010711

NOVELTY - Increasing **expression** of a protein in a mammalian cell culture in aqueous medium, comprising adding to the medium at least one solute which inhibits cell growth or density at a higher than optimal concentration, is new. The solute increases the cell stress in the absence of prior adaptation to the increased **solute stress** and protein **expression** is increased while cells are subjected to the stress.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) determining solute concentration solute concentration in a cell culture medium to produce the highest protein product **expression** from a cell, where the culture medium has all the requirements necessary for optimal growth, comprising:

(a) determining the concentration of the solute necessary for optimal cell growth;

(b) increasing the concentration of the solute to a concentration above the optimal for cell growth, thus placing the cells under increased **solute stress**; and

(c) determining the concentration, which provides increased protein product **expression** in the absence of prior adaptation of the cells to increased **solute stress**;

(2) recovering antibodies from hybridoma cells grown in a growth medium, by:

(a) growing the cells in the growth medium in the presence of at least one solute which is present at a concentration sufficient to increase **solute stress** upon the cells to inhibit cell growth or density and enhance **expression** of the antibody; and

(b) recovering the antibody from the medium containing the solute.

USE - The method is useful for increasing the **expression** of a protein in a mammalian cell culture, particularly in increasing antibody production from hybridoma cell lines. The antibodies may be used in the study of cell surface antigens, for affinity purification of proteins, histocompatibility testing, studying various viruses, radioimmunoassay, drug targeting and immunotherapy.

Dwg.0/3

TI Increasing protein **expression** in a cell culture, useful for increasing antibody production, comprises adding to the cell medium a solute inhibiting cell growth or density in an amount above the amount needed for optimal cell growth.

L15 ANSWER 16 OF 24 WPIDS (C) 2002 THOMSON DERWENT

IN HOWARTH, W; INLOW, D; MAIORELLA, B

AN 1989-178386 [24] WPIDS

CR 2001-366475 [38]

AB WO 8904867 A UPAB: 20010711

Determining the optimal level of prod **expression** in animal cell culture in which the concn of a solute of interest in a culture medium compsn for optimal prod **expression** is different than the culture medium compsn detd for optimal cell growth, comprises (a) growing the animal cell culture in a medium to determine optimal cell growth, (b) varying concn of the solute in the culture medium to a concn above that optimal for cell growth, effective to create an environment of **solute stress** on the cell culture, (c) monitoring the prod **expression** under the varying solute concn conditions to determine optimal prod **expression** and (d) selecting the solute concn that provides the optimal combination of cell growth and prod **expression** which allows for optimal productivity.

The solute may be an inorganic salt or ion, e.g. NaCl or KCl, a metabolite, e.g. lactate or ammonium or an organic polyol. Also claimed is a method of increasing the prodn of monoclonal antibodies (MAbs) during mammalian cell culture comprising culturing hybridoma cells under conditions of **solute stress**.

ADVANTAGE - Creating an environment of controlled **solute stress** can favour an increase in specific (per cell) prod **expression** and/or increase culture longevity.

Dwg.0/2

TI Determining optimal prod. **expression** in animal cell culture - by varying solute concn. from that which is optimal for cell growth.

L15 ANSWER 17 OF 24 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

AN 1989-11002 BIOTECHDS

AB A new method for determining the optimal level of product **expression** in animal cell culture comprises altering the concentration of a solute contained in a culture medium so that it is not optimal for cell growth. The animal cell culture is grown in a culture medium to determine the concentration of the solute which is optimal for growth, and the concentration of this solute is then increased to a value above this cell growth optimum to induce **solute stress** and optimize the production of cell products. The product **expression** is monitored and the solute concentration which is optimal for product formation is selected and used in further cell cultures. The animal cell culture is preferably of mammalian origin, especially a hybridoma culture (D-234, ATCC HB-8598; T-88, ATCC HB-9543; T-88, ATCC HB-9431), that produces IgM monoclonal antibodies. The solute is preferably an inorganic salt or an inorganic ion, especially NaCl or KCl or is a metabolite, especially lactate, ammonium or organic polyols.

When culturing T-88 and D-234 cells the optimal NaCl concentration is 400-450 and 350-400 mOsm/kg, respectively. (35pp)

TI Determining the optimal product **expression** in animal cell culture, e.g. monoclonal antibody production by hybridoma culture; by varying a solute concentration from that which is optimal for cell growth

L15 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2002 ACS

SO Ger. Offen., 8 pp.

CODEN: GWXXBX

IN Galinski, Erwin A.; Louis, Petra

AB A method of improving the tolerance of a mesophilic organism or cell line to biol. stresses, esp. dehydration, by introduction of the genes from extremophiles for synthesis of solutes that endow stress tolerance are described. In addn. to allowing the synthesis of these solutes, such as ectoine, under moderate conditions, the improved stress tolerance allows increased yields and productivity, esp. of foreign proteins. Transformation of Escherichia coli with the genes for ectoine synthase of Marinococcus halophilus resulted in cells accumulating ectoine. These cells were able to grow in 5% NaCl.

TI Increasing the stress tolerance of an organism by transformation with extremophile genes for biosynthesis of solutes that increase stress tolerance

L15 ANSWER 19 OF 24 FEDRIP COPYRIGHT 2002 NTIS

SUM 1) Identify physiological adaptations that occur when soil bacteria are exposed to matric water stress. 2) Identify genes that contribute to matric stress tolerance as well as to determine how those genes are regulated. 3) Determine how matric stress affects bacterial growth and survival and whether matric water stress adaptation affects tolerance towards other stresses bacteria encounter in soil. The goal of this research is to determine how matric water stress affects bacteria, the mechanisms bacteria employ to respond to this stress, and how tolerance mechanisms may affect important bacterial processes such as biodegradation or plant-microbe interactions. Because of the various environmentally important traits of Pseudomonas putida, such as the ability of various strains to degrade environmental pollutants or promote plant growth, it will be used as a model organism. The matric water potential of the culture medium will be lowered with polyethylene glycol (PEG), which is preferable to more traditional methods of manipulating the water content of soils or the salt concentration of soil slurries since they do not permit the ability to differentiate between the effect of lowered matric water potential, reduced substrate supply, and reduced water content on microorganisms. Dehydration of the cell envelope is much greater with a matric than an osmotic stress and consequently emphasis will be placed on identifying the physiological and genetic mechanisms that contribute to maintaining an intact and functional cell envelope. Determining whether the mechanisms for matric stress tolerance are unique or part of a common stress response is critical to this study since many other environmental stresses also affect the integrity and function of cell envelopes. PR identify matric-stress responsive genes that encode cell envelope constituents in Pseudomonas putida and to determine whether these genes play a role in matric stress tolerance. Furthermore, we have initiated a comprehensive characterization of the biofilm exopolysaccharides (EPS) produced under osmotic and matric stress conditions. The central hypothesis of the research is that the response mechanisms to water deprivation imposed by a matric stress is fundamentally different from a **solute stress** response mechanism. Genes encoding cell envelope constituents that are responsive to water deprivation were identified in Pseudomonas putida by creating translational fusions with miniTn5phoA. Preliminary observations indicate that genes encoding cell envelope proteins are differentially expressed under conditions that simulate matric and **solute stress** under laboratory conditions. Furthermore, the magnitude of water deprivation severity strongly influences the **expression** of some



of the tagged genes and survival of the mutants. We have been using arbitrary primed polymerase chain reaction techniques to isolate DNA adjacent to the gene fusion and are in the process of sequencing that DNA to identify the target gene by comparing that sequence to the genomic database sequence of *P. putida*; the *P. putida* genome is being sequenced by The Institute of Genomic Research. We have also determined that more EPS is produced under matrix than **solute stress** or when water is not limiting growth conditions. Biofilms generated under matrix stress appear to preferentially produce more low molecular weight carbohydrates and increase the amount of high molecular weight alginate while not changing the amount of a high molecular weight acidic polysaccharide which is presumably galactoglucan. The hydroscopic nature of these polysaccharides may create a more hydrated microenvironment around the cell than the bulk environment possibly to stabilize dehydrated membranes. A genetic approach will be pursued to identify the genes regulating EPS production and to determine how mutants deficient in EPS production survive dehydration and whether EPS production helps stabilize membrane integrity. We are using the unfinished *P. putida* genome sequence to identify potential EPS biosynthesis genes and to develop strategies for site-specific mutagenesis to create null mutants. In conclusion, this work has established a foundation for understanding the complex adaptive strategies bacteria employ for responding to matrix water stress and for highlighting how those response mechanisms differ from those employed for responding to **solute stresses**. PB and non-permeating solutes on the fatty acid composition of *Pseudomonas putida*. Applied and Environmental Microbiology 66(6):2414-2421.

TI MATRIC WATER STRESS TOLERANCE BY SOIL BACTERIA

L15 ANSWER 20 OF 24 LIFESCI COPYRIGHT 2002 CSA

SO (20010529) . US Patent: 6238891; US CLASS: 435/70.21; 435/69.1; 435/70.1; 435/252.3; 435/326; 530/386; 530/388.1; 530/388.15; 530/412.

AU Maiorella, B.; Inlow, D.; Howarth, W.

AB A method of determining the optimal level of product **expression** and cell growth of animal cell culture is described. The method generally comprises culturing cells under conditions of **solute stress**, that is, under conditions whereby optimal cell growth or growth rate is decreased yet levels of product **expression** are increased. In a preferred embodiment of the invention is described a method of increasing the yield of monoclonal antibodies comprising culturing hybridoma cells in an environment of **solute stress**. One approach to the creation of such an environment is the addition of inorganic salts, organic polyols, or metabolic products to the culture medium. One- to three-fold increases in antibody yield have been obtained by these methods.

TI Method of increasing product **expression** through **solute stress**

L15 ANSWER 21 OF 24 COMPENDEX COPYRIGHT 2002 EEI

SO Acta Metall v 37 n 8 Aug 1989 p 2261-2265

CODEN: AMETAR ISSN: 0001-6160

PY 1989

AU Brechet, Y.J.M. (McMaster Univ, Hamilton, Ont, Can); Dryden, J.R.; Purdy, G.R.

AN 1990(4):38643 COMPENDEX DN 900439882

AB The diffusion induced migration of a wall of edge dislocations is considered. The dislocations are assumed to be fast diffusion pipes, connected at their ends to solute sinks, and in equilibrium with these sinks along their lengths. We find that the array of edge dislocations is stabilized by the long range **solute stress** field (a solute misfit is necessary), and is capable of synchronous climb in response to local **solute stress** fields. The climb of the dislocation wall acts to channel solute to the sinks, in close analogy with chemically induced grain boundary migration. **Expressions** are derived for the climb force on a single dislocation, and on the dislocations in the wall. The stability of the migrating wall as a function

of dislocation spacing and velocity is discussed. (Author abstract) 6 Refs.  
 TI Diffusion induced motion of a wall of dislocations.

L15 ANSWER 22 OF 24 INSPEC COPYRIGHT 2002 IEE  
 SO Acta Metallurgica (Aug. 1989) vol.37, no.8, p.2261-5. 6 refs.  
 Price: CCCC 0001-6160/89/\$3.00+0.00  
 CODEN: AMETAR ISSN: 0001-6160  
 AU Brechet, Y.J.M.; Dryden, J.R.; Purdy, G.R. (Dept. of Mater. Sci. & Eng.,  
 McMaster Univ., Hamilton, Ont., Canada)  
 AN 1989:3485896 INSPEC DN A89134889  
 AB The diffusion induced migration of a wall of edge dislocations is  
 considered. The dislocations are assumed to be fast diffusion pipes,  
 connected at their ends to solute sinks, and in equilibrium with these  
 sinks along their lengths. The authors find that the array of edge  
 dislocations is stabilized by the long range **solute**  
**stress** field (a solute misfit is necessary), and is capable of  
 synchronous climb in response to local **solute stress**  
 fields. The climb of the dislocation wall acts to channel solute to the  
 sinks, in close analogy with chemically induced grain boundary migration.  
**Expressions** are derived for the climb force on a single  
 dislocation, and on the dislocations in the wall. The stability of the  
 migrating wall as a function of dislocation spacing and velocity is  
 discussed.  
 TI Diffusion induced motion of a wall of dislocations.

L15 ANSWER 23 OF 24 EUROPATFULL COPYRIGHT 2002 WILA  
 SO Wila-EPS-1996-H11-T1  
 IN HOWARTH, William, 5933 East Castro Valley Boulevard, Castro Valley, CA  
 94552, US;  
 MAIORELLA, Brian, 5661 Broadway, Oakland, CA 94618, US;  
 INLOW, Duane, 630 Mariposa Avenue, 310, Oakland, CA 94610, US  
 TIEN CELL CULTURE MEDIUM FOR ENHANCED CELL GROWTH, CULTURE LONGEVITY AND  
 PRODUCT **EXPRESSION**.

L15 ANSWER 24 OF 24 PATOSWO COPYRIGHT 2002 WILA  
 WOAI PCT-PUBLICATION  
 SO PCT-GAZETTE-890601  
 IN MAIORELLA, BRIAN, US;  
 INLOW, DUANE, US;  
 HOWARTH, WILLIAM, US  
 TI METHOD OF INCREASING PRODUCT **EXPRESSION** THROUGH **SOLUTE**  
**STRESS**.

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